

The effect of nicotine on oral health

Grzegorz Trybek^{1 ABDEG}, Magda Aniko-Włodarczyk^{1 BDEF}, Olga Preuss^{1 BDF},
Piotr Kuligowski^{1 BF}, Ewa Gabrysz-Trybek^{2 DF},
Aleksandra Suchanecka^{2 DF}, Patryk Niewczas^{3 F}, Anna Grzywacz^{2 DEF}

Authors' Contribution:

A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

¹ Department of Oral Surgery, Pomeranian Medical University in Szczecin, Szczecin, Poland

² Independent Laboratory of Health Promotion, Pomeranian Medical University in Szczecin, Szczecin, Poland

³ Faculty of Physical Education, University of Rzeszów, Rzeszów, Poland

abstract

Background: Nicotine absorbed by the skin and also by the digestive, respiratory and excretory systems is one of the most known toxins found in tobacco. This work reviews available literature on the influence of nicotine on human health, and in particular on the oral cavity.

Material/Methods: A review of literature related to the topic of the paper.

Results: Numerous studies indicate that nicotine adversely affects human health. It exerts a negative effect at the cellular level by modifying metabolism, and disturbs the interactions between tissues, which strongly promotes the formation of cancer-like changes. Nicotine causes numerous pathologies in the respiratory, immune, and cardiovascular systems leading to a number of metabolic disorders.

Conclusions: The intake of nicotine contained in tobacco products has a particularly negative effect on the oral cavity. It accelerates periodontitis, with weaker clinical symptoms associated with resistance to conventional treatment. In addition, nicotine changes the oral cavity microflora, increasing the amount of harmful bacteria and pathogenic fungi.

Key words: tobacco, nicotine, oral health.

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Corresponding author: Magda Aniko-Włodarczyk, Al. Powstańców Wlkp. 72/18, 70-111 Szczecin, tel.: 91-466-17-36, e-mail: magdaniko@wp.pl

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INTRODUCTION

Tobacco has been known to man for many thousands of years, but its use in Europe started after the discovery of America by Christopher Columbus in 1492. First brought to Spain by monk Roman Pano, tobacco gained in popularity in the sixteenth century. After the successful treatment of the migraine headaches suffered by the French queen Catherine de Medici by diplomat Jean Nicot, it began to be known as nicotiana [1]. Hence the English name 'nicotine' used for the tobacco's best-known active alkaloid, first extracted in 1828 by L. Reimann and W.H. Posselt, chemistry students at the University of Heidelberg.

In the last five hundred years, tobacco has been consumed in a variety of forms. Initially, people chewed unprocessed green tobacco leaves, then they started to sniff powdered leaves (snuff), and from the seventeenth century dried tobacco leaves have been smoked as cigars, cigarettes or in pipes [2, 3]. Less popular uses include ointments against parasites, eye drops, and infusions [4, 5].

The consumption of tobacco products is one of the best documented causes of various diseases. Scientific knowledge about their harmfulness has been gathered mainly over the last 60 years. According to the World Health Organization (WHO), tobacco kills half of its users, about 7 million a year, of which 6 million are active smokers and 1 million are passive. It is estimated that 1 billion people in the world population smoke tobacco. WHO considers tobacco smoking an epidemic and a chronic disease [6, 7].

Tobacco smoke contains more than four thousand components, most of which are considered toxic, both as gas (volatile) and in molecular (solid) phases. The gas phase mainly comprises nitrogen, oxygen, carbon monoxide, carbon dioxide, ammonia, hydrogen cyanide, formaldehyde, acetaldehyde, pyridine and nitrosamines, while the solid phase is primarily the pharmacologically active alkaloid - nicotine, as well as turpentine, fatty acid esters, aromatic and aliphatic hydrocarbons, which comprise tar. Of course, this list includes only the most significant components as the gas phase comprises about 3,500 components and the solid phase 500 [8]. Nowadays, there are also other products containing nicotine, like chewing gums, patches, vaporizers. Although they do not contain the toxins, they still contain nicotine.

The aim of this literature review was to show the harmful effect of nicotine.

MATERIAL AND METHODS

The publications used in this work were sourced from the PubMed database and Google Scholar. We searched for the effect of nicotine on general health and the oral cavity. The index entries used to search the PubMed and Google Scholar browsers included tobacco, nicotine, oral health, periodontitis, neoplasms, leukoplakia, and collagen. The work uses articles published in English and Polish.

NICOTINE

Nicotine is a substance with the chemical formula $C_{10}H_{14}N_2$, and the structural formula shown in Figure 1.

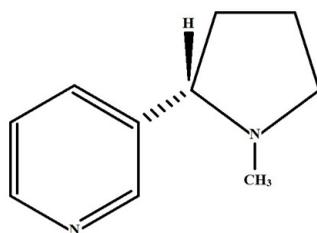


Fig. 1. Structural formula of nicotine

Figure 1 shows the chemical structure of nicotine. A strong alkaloid (amine) with a characteristic smell, nicotine can be absorbed by the respiratory and digestive systems, as well as through the skin. It binds to plasma proteins, crosses the placental barrier and passes into breast milk. Absorption by mucous membranes depends on pH; the higher pH, the greater the lipophilicity and the ability of active resorption by biological membranes [9]. Nicotine metabolism takes place in the liver in two stages. The first one consists of microsomal oxidation to metabolites such as cotinine, nornicotine, dimethylketinins and methylamino-butyric acid. In the second stage, metabolic products are glucuronidated and excreted with urine, feces, bile, saliva and sweat [10, 11]. Nicotine causes a number of harmful effects:

- Addiction – nicotine is one of the most addictive substances, both in psychological and physiological terms. Nicotine reacts with acetylcholine receptors and stimulates dopaminergic transmission. This, in turn, improves mood and cognitive functions. Chronic stimulation of GABAergic neurons results in elimination of the inhibitory action of dopamine, which strengthens addiction [12].
- Metabolic disorders – nicotine increases the production of catecholamines by stimulation of the autonomic system. It increases glycogen synthesis due to the stimulation of α -adrenergic receptors, reducing fasting glucose levels. It also intensifies lipolysis leading to a reduction in body mass. Nicotine causes insulin resistance, predisposing to the metabolic syndrome [13].
- Carcinogenesis – nicotine promotes tumor angiogenesis and tumor growth. It leads to mutations within the cell's DNA. It acts synergistically with other carcinogens, shortening the period of tumor growth and inhibits the apoptotic process [14, 15]. Nicotine is one of the causes of lung, breast, intestine and pancreatic cancers [16].
- The cardiovascular system – nicotine has a sympathomimetic effect on the hemodynamics of this system. The effects are more pronounced with high intakes of nicotine over a short period. Stimulation of the adrenergic system leads to accelerated heart work, increased cardiac contractility, and increased blood pressure. Nicotine reduces blood flow through coronary and cutaneous vessels. It indirectly limits the supply of oxygen to the myocardium. However, it increases the blood flow through the skeletal muscle [17].

- Respiratory system - nicotine directly affects the lung tissue and indirectly influences the respiratory pattern through the central nervous system. It causes emphysema, reduces the flexibility of the pulmonary parenchyma, increases the volume of alveoli and airway resistance [18].
- The immune system - nicotine acts immunosuppressively on the immune system, reducing the immune response. It affects a reduction in the T cell population, causes macrophage dysfunction, and delays the healing process by reducing cell adhesion to the epithelium. Nicotine affects the functioning of the hypothalamic-pituitary-adrenal axis through the sympathetic and parasympathetic systems, thus inhibiting the immune system. A nicotine-induced increase in adrenocorticotrophin secretion also suppresses the immune system [19].
- The sense of sight - in smokers, nicotine is more likely to cause macular degeneration than in non-smokers. In people with diabetes, nicotine accelerates clouding of the eye lens. It may intensify cataract formation [20].
- The digestive system - nicotine can be the cause of gastroesophageal reflux or gastric ulcers. It causes an increase in gastric acid secretion. It relaxes the smooth muscle by increasing the production of endogenous nitric oxide. Smokers have an increased resistance to treatment of the infection of *Helicobacter pylori* [21].
- Excretory system - nicotine increases the risk of chronic kidney disease. Nicotine users have increased albumin excretion in urine, as nicotine reduces the glomerular filtrate [22].
- Collagen production - type I collagen is one of the most important building proteins in the human body. It consists of a combination of two pro $\alpha 1$ chains linked by a pro $\alpha 2$ chain. Nicotine dramatically decreases the synthesis of the mRNA responsible for pro $\alpha 1$ synthesis in collagen-producing fibroblasts. Nicotine increases the amount of mRNA producing metalloproteinases and increases their enzymatic activity. Metalloproteinases are zinc ion dependent endoenzymes produced by fibroblasts. They include collagenases, enzymes that break down collagen. [23, 24].

Smoking tobacco and the consumption of other tobacco products have adverse systemic effects and also affect the condition of the directly exposed oral cavity and nasopharynx. This action is associated with thermal and chemical injury from exposure to tobacco smoke. Nicotine addiction is a cause in the development of periodontal disease, caries, and pre-cancerous conditions such as leukoplakia, pathological changes in the mucous membranes or tongue, as well as tumors. Effects on oral health are summarized in Table 1.

Table 1. The impact of tobacco consumption on oral health

The effects of nicotine addiction on oral health	
Oral cavity	Halitosis, taste and smell disorders, stomatitis, black hairy tongue, candidiasis, leukoedema, precancerous lesions, leukoplakia, cancer
Periodontium	Deepening of the gingival pockets, deposition of supragingival and subgingival plaque, loss of connective tissue attachment and alveolar bone, periodontal disease
Teeth	Numerous caries foci, discoloration, tooth loss

DEVELOPMENT OF NEOPLASMS

Nicotine addiction is one of the most significant risk factors of tumors in the oral cavity and nasopharynx [25]. Nicotine metabolites modify proteins and nucleic acids in cells, which is directly responsible for the development of oral tumors [26]. Nicotine influences the formation of cancerous changes by protecting cancer cells against apoptosis and creating an immunosuppressive environment [26]. Inhibiting the body's immune response involves compromising immune cell chemotaxis and reducing antibody production.

Leukoplakia is a white lesion in the mouth that cannot be scratched off and is not part of another disease. Undoubtedly, nicotine addiction is the most significant risk factor of leukoplakia in the oral cavity [27]. In the histopathological picture, it first assumes the form of acanthosis and hyperkeratosis. Hyperkeratosis, depending on the presence of the cell nucleus, takes the form of parakeratosis, orthokeratosis or both at the same time. When left untreated for a long time, it may show atypical and cellular dysplasia in a microscopic image, with a very high chance of neoplastic metaplasia. Most often, leukoplakia appears on the mucous membrane of the cheek, the bottom of the mouth and on the tongue [28]. Different studies show that the risk of neoplastic transformation of leukoplakia varies from 3.73% to 29% [28, 29, 30, 31]. Leukoplakia should be distinguished from the very similar leukoedema, usually blue, white or gray, most often appearing on the mucous membrane of the cheek without any clinical symptoms [32]. Unlike leukoplakia, it retains elasticity and is not associated with deformation [33]. Leukoedema is not dangerous and does not require any medical intervention.

Impairment of tissue regeneration - chronic nicotine addiction has a negative effect on the process of wound healing in the oral cavity [34]. This process causes tissue ischemia and a reduction in the number of newly formed blood vessels, which directly impairs bone regeneration [35]. In addition, nicotine metabolites have the ability to bind to fibroblasts and osteoblasts. They disrupt cell transport and fibroblast adhesion as well as osteoblast adhesion. These substances also hinder the maturation of erythrocytes and their precursors, resulting in changes in blood flow [36]. Dry socket, a complication following tooth extraction, is four times more common in people who smoke [37].

Effects on the oral microenvironment - smokers usually show symptoms of poor oral hygiene very early, a direct result of changes in the biochemical composition and physical properties of saliva. Nicotine and other factors reduce saliva pH while the concentrations of calcium and phosphorus ions increase, resulting in an amount of supragingival and subgingival calculus [38, 39]. Cigarette smokers also have problems in the detection of flavors and aromas [40]. Nicotine impairs the detection of bitter and salty flavors most, but has almost no effect on the perception of sweet taste [40].

Soft tissues - nicotine addiction results in significantly deteriorated periodontitis. It causes loss of connective tissue attachment and resistance to treatment [41], and periodontitis with a lower rate of bleeding when probing than in healthy people, despite poorer hygiene [42]. In addition, chronic nicotine addiction greatly affects the risk of tooth loss and an increase in connective tissue loss [43]. Nicotine can also often lead to dryness of the mouth - xerostomia. This condition contributes to the occurrence of black hairy tongue [44], directly caused by chemical and thermal irritation of

the oral mucosa. This disease is characterized by the occurrence of black discolorations, hyperplasia and hyperkeratosis of filamentous warts. Nicotinism also affects a change in the oral microflora. Nicotine increases the accumulation of *Candida* fungi in the oral cavity [45]. Excessive growth of these fungi may cause candidiasis, rhomboiditis, and inflammation of the mouth [46]. Nicotinism during pregnancy is a significant risk factor affecting congenital malformations, such as cleft palate or lip.

CONCLUSIONS

Nicotine, found primarily in tobacco products, is a highly addictive substance. Together with its metabolic products, it exerts many adverse effects both within the oral cavity and the entire human body. Nicotine can cause local inflammation in the mouth, serious metabolic changes, and also neoplasms – an immediate threat to life. It is a risk factor for many diseases, and its negative effects can persist for many years after quitting the nicotine addiction.

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